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N-LITHIO-*N*-(2-LITHIOETHYL)- AND *N*-LITHIO-*N*-(3-LITHIOPROPYL)-BENZAMIDE: DIRECT PREPARATION AND SYNTHETIC APPLICATIONS OF 2-LITHIOETHYL- AND 3-LITHIOPROPYL-AMINE EQUIVALENTS

José Barluenga,* Francisco Foubelo, Francisco J. Fañanás

Departamento de Química Organometálica, Facultad de Química,
Universidad de Oviedo, 33071 Oviedo, Spain

and

Miguel Yus

División de Química Orgánica, Facultad de Ciencias,
Universidad de Alicante, 03690 Alicante, Spain

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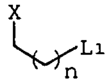
Summary: The successive reaction of 2-chloroethyl and 3-chloropropyl-benzamide with n-butyl-lithium and lithium naphthalenide at temperatures ranging between -78 and -50°C leads to *N*-lithio-*N*-(2-lithioethyl)- and *N*-lithio-*N*-(3-lithiopropyl)benzamide [(8), (9)], which by treatment with different electrophiles (H_2O, D_2O, Me_2S_2, CO_2, Pr^iCHO, PhCHO, Me_2CO, Ph_2CO, and O_2) yields the expected functionalized benzamides [(10), (11)]. The acidic and basic hydrolysis of compounds (10) and (11) gives different results depending on the structure of the substrate and the reaction conditions.

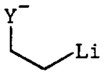
Introduction

Functionalized organolithium compounds (1) are interesting intermediates in organic synthesis due to their ability to transfer functionality by reaction with electrophilic reagents. The stability of such intermediates depends strongly on the relative position of the metal atom and the function: whilst the β-functionalized systems[1] (1, n = 1) are very unstable species and decompose by β-elimination yielding olefins[2] as the main products, the corresponding γ-,[3] δ-,[4] or ε-functionalized[5] derivatives (1, n = 2-4) are more stable and they can be considered, in general, as typical organolithium reagents. In the case of the β-substituted compounds the stability is greatly increased (a) where the oxygenated or nitrogenated function at the β-position bears a negative charge (2),[2b,6] so the loss of electronegativity in the heteroatom difficults the elimination, and (b) where the lithium atom is attached to a

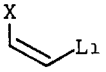
sp^2 hybridized carbon atom [(**3**), (**4**)].[7]



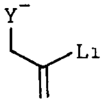
(**1**)



(**2**)



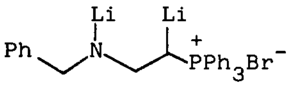
(**3**)



(**4**)

n = 1-4
X = Hal, OR, NR_2,...
Y = O, NR

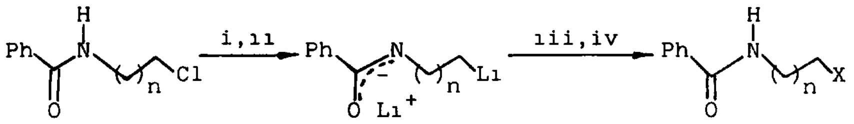
The most general method for the preparation of oxygenated and nitrogenated intermediates of the type (**2**) involves β-substituted organomercurials.[8] Only for Y = O the mercury route can be avoided, so, oxygenated derivatives of the type (**2**) have been recently prepared directly from chlorohydrins,[9] epoxides,[10] or ketones;[6] these methodologies fail for Y = NR. In our hands only the intermediate (**5**), with actually is an ylide, has been prepared by a direct method: double lithiation of the adequate precursor with n-butyl-lithium.[11] In the present paper we described a new way to prepare directly an aminated intermediate of the type (**2**) and its γ-homologated derivative, which are useful synthons for the units $H_2N(CH_2)_nCH_2^-$, n = 1, 2.[12]



(**5**)

Results and Discussion

The successive treatment of *N*-(2-chloroethyl)benzamide (**6**) with n-butyl-lithium and lithium naphthalenide at -78°C led to the β-substituted organolithium intermediate (**8**). The *in situ* reaction of this dianion with different electrophilic reagents (water, deuterium oxide, dimethyl disulphide, carbon dioxide, aldehydes or ketones, and oxygen) yielded the expected β-substituted *N*-ethylbenzamides (**10**). (Scheme 1 and Table 1, entries 1-9). The more stable γ-substituted organolithium intermediate (**9**) could be prepared and reacted at temperatures ranging between -50 and -30°C using the same method as for (**8**). The *in situ* treatment of this dianionic species with the same variety of electrophiles as above afford the corresponding γ-substituted *N*-propylbenzamides (**11**). (Scheme 1 and Table 1, entries 10-17).



(6); n = 1
(7); n = 2

(8); n = 1
(9); n = 2

(10); n = 1
(11); n = 2
a; X = H
b; X = D
c; X = MeS
d; X = CO_2H
e; X = Pr^iCHOH
f; X = PhCHOH
g; X = Me_2COH
h; X = Ph_2COH
i; X = OH

Scheme 1. *Reagents and conditions:* i, Bu^nLi, -78 (n = 1) or -50°C (n = 2); ii, $Li^+C_{10}H_8^-$, -78 (n = 1) or -50 to -30°C (n = 2); iii, Electrophile E^+ = H_2O, D_2O, Me_2S_2, CO_2, Pr^iCHO, PhCHO, Me_2CO, Ph_2CO, O_2, -78 to 20°C; iv, H_2O.

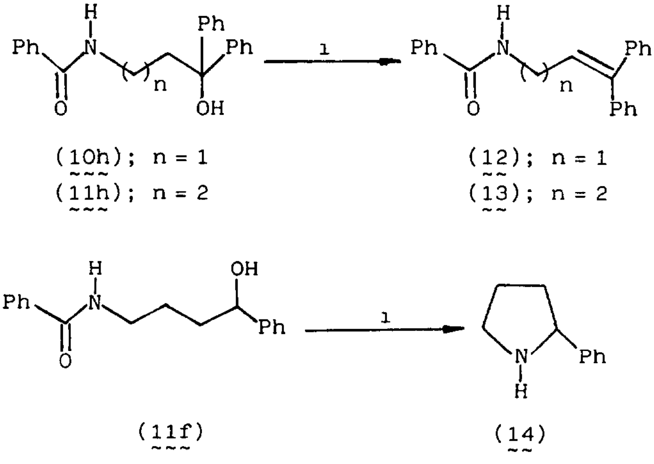
Table 1. Preparation of intermediates (8) and (9) and their reaction with electrophiles. Isolation of products (10) and (11).

Entry	Starting amide		Lithium	Electrophile	Product		
	no.	n	dianion	E^+	no.	Yield (%)[a]	m.p. (°C)[b] or b.p. (°C)/mmHg
1	(6)	1	(8)	H_2O	(10a)	91	112-114/0.1[c]
2	(6)	1	(8)	D_2O	(10b)	88	112-114/0.1
3	(6)	1	(8)	Me_2S_2	(10c)	86	118-120/0.001[d]
4	(6)	1	(8)	CO_2	(10d)	64	116-118[e]
5	(6)	1	(8)	Pr^iCHO	(10e)	72	106-108
6	(6)	1	(8)	PhCHO	(10f)	72	84-86[f]
7	(6)	1	(8)	Me_2CO	(10g)	74	105-107[g]
8	(6)	1	(8)	Ph_2CO	(10h)	71	145-147
9	(6)	1	(8)	O_2	(10i)	65	154-156/0.1[h]
10	(7)	2	(9)	H_2O	(11a)	94	79-80[i]
11	(7)	2	(9)	D_2O	(11b)	88	79-80
12	(7)	2	(9)	Me_2S_2	(11c)	82	123-125/0.001[j]

Entry	Starting amide		Lithium	Electrophile	Product		
	no.	n	dianion	E^+	no.	Yield (%)[a]	m.p. (°C)[b] or b.p. (°C)/mmHg
13	(7)	2	(9)	CO_2	(11d)	66	77-79[k]
14	(7)	2	(9)	Pr^iCHO	(11e)	68	148-150/0.001
15	(7)	2	(9)	PhCHO	(11f)	73	oil[l]
16	(7)	2	(9)	Me_2CO	(11g)	71	146-148/0.001
17	(7)	2	(9)	Ph_2CO	(11h)	81	157-159

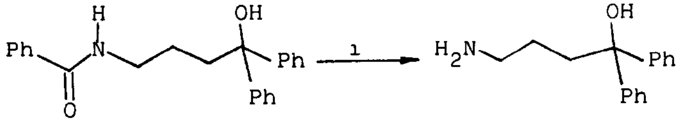
[a] Isolated yield based on the starting materials (6) or (7). [b] From hexane/$CHCl_3$. [c] Lit.,[13] b.p. 285°C/745 mmHg. [d] Lit.,[14] m.p. 57°C. [e] Lit.,[15] m.p. 120°C. [f] Lit.,[16] m.p. 85-86°C. [g] Lit.,[17] m.p. 106-107°C. [h] Lit.,[14] m.p. 66-67°C. [i] Lit.,[18] m.p. 83°C. [j] Lit.,[19] b.p. 184-185°C/1 mmHg. [k] Lit.,[20] m.p. 79-80°C. [l] R_F 0.42 [silica gel, THF-hexane (3:2)].

The results of the hydrolysis of the amide moiety in products (10) and (11) depends strongly on the structure of the substrate and on the reaction conditions. The acidic hydrolysis led to the corresponding dehydratation where the formed carbon-carbon double bond is very conjugated; so, starting from compounds (10h) or (11h) the corresponding olefins (12) and (13) were exclusively isolated by treatment with sulphuric acid, in which the amide group did not suffers hydrolysis. On the other hand when the same process was carried out on compound (11f) the corresponding 2-phenylpyrrolidine (14) was obtained , arisen from the intramolecular dehydratation of the intermediate aminoalcohol. (Scheme 2).



Scheme 2. *Reagents:* i, H_2SO_4-EtOH-dioxane

The difficulties found by the acid hydrolysis of (10h) and (11h) have been overcome using basic conditions. So, for instance, starting from (11h) the treatment with potassium hydroxide led to expected aminoalcohol (15). (Scheme 3).



(11h) (15)

Scheme 3. *Reagents:* i, KOH-EtOH-H_2O-dioxane

From the results described in this paper, we conclude that this methodology represents an useful way to introduce the unit $H_2N(CH_2)_nCH_2^-$ (n = 1, 2) in an electrophilic reagent.

Experimental

General.- M.p.s are uncorrected and were measured on a Buchi-Tottoli capyllary melting point apparatus. I.r. spectra were determined with a Perkin-Elmer 298 spectrometer. ^1H and ^{13}C N.m.r. spectra were recorded on a Varian FT-80 spectrometer with $SiMe_4$ as internal standard in $CDCl_3$ as solvent. M.s. (e.i.) were recorded with a Hewlet-Packard 5987A spectrometer. The purity of volatile distilled products and the chromarographic analysis were determined with a g.l.c. Varian Aerograph 2800 instrument equipped with OV-101 Chromosorb column. Elemental analysis were carried out with a Perkin-Elmer 240 Elemental Analyzer. Starting reactants were of the best commercial grade available and were used without further purification. n-Butyl-lithium[21] and lithium naphthalenide[22] were prepared as already described. Ether (refering to diethyl ether) was dried successively with anhydrous calcium chloride, sodium sulphate, sodium, and a K-Na (K_3Na) liquid alloy[23] under argon reflux, and was then distilled and stored under argon. Tetrahydrofuran (THF) was dried successively with anhydrous calcium chloride and sodium sulphate; it was then refluxed with potassium, distilled, and stored under argon. All reactions (except the preparation of the starting materials and the acidic and basic hydrolysis) were carried out under argon and the glassware were dried before use.

Preparation of Intermediates (8) *and* (9) *and Reaction with Electrophiles. General Procedure.*- To a solution of *N*-(2-chloroethyl)benzamide (6)[13] (0.92 g, 5 mmol) or *N*-(3-chloropropyl)benzamide (7)[18] (0.98 g, 5 mmol) in tetrahydrofuran (25 ml) was added an ethereal solution of n-butyl-lithium (5 mmol) at -78 (n = 1) or -50°C (n = 2) under argon and stirring was continued for 20 min at the same temperature. To the resulting mixture was added a solution of lithium naphthalenide in tetrahydrofuran (11 mmol) and it was stirred for 4 h at -78 (n = 1) or at temperatures ranging between -50 and -30°C (n = 2). The mixture was cooled at -78 °C and the corresponding electrophile (5 mmol) was then added and it was stirred overnight allowing the temperature to rise to 20 °C . The resulting mixture was hydrolyzed with water and extracted with ether. The organic layer was dried (Na_2SO_4) and evaporated (15 mmHg). Naphthalene was removed in vacuo (0.001 mmHg; 50 °C bath temperature) and the resulting residue was purified by flash column chromatography, distillation, or recrystallization.

N-*Ethylbenzamide* (10a)^{13} ν_{max} (neat) 3310 (NH) and 1630 (C=O) cm^{-1}; δ_H 1.2 (3 H, t, *J* 7 Hz Me), 3.4-3.6 (2 H, m, CH_2), 6.35-6.65 (1 H, br signal, NH), and 7.3-8.1 (5 H, m, ArH); δ_C 14.9 (Me), 35.1 (CH_2), 127.5, 128.7, 131.6, 135.7 (ArC), and 168.9 (C=O) ppm; *m/z* 149 (*M*$^+$, 21%), 106 (11), 105 (100), 77 (48), 51 (14), and 32 (18).

N-(2-*Deuterioethyl)benzamide* (10b) ν_{max} (neat) 3310 (NH) and 1630 (C=O) cm^{-1}; δ_H 1.2 (2 H, t, *J* 7 Hz, CH_2D), 3.5 (2 H, q, *J* 7 Hz, CH_2N), 6.35-6.65 (1 H, br signal, NH), and 7.3-8.1 (5 H, m, ArH); δ_C 14.8 (t, J_{CD} 19.5 Hz, CH_2D), 35.1 (CH_2N), 127.5, 128.7, 131.6, 135.7 (ArC), and 168.9 (C=O) ppm; *m/z* 150 (*M*$^+$, 19%), 106 (13), 105 (100), 77 (51), 51 (11), and 32 (18).

N-(2-*Methylthioethyl)benzamide* (10c)^{14} ν_{max} (Nujol) 3320 (NH) and 1630 (C=O) cm^{-1}; δ_H 2.1 (3 H, s, Me), 2.7 (2 H, t, *J* 6.5 Hz, CH_2S), 3.7 (2 H, q, *J* 6.5 Hz, CH_2N), 6.7-7.0 (1 H, br signal, NH), and 7.3-8.1 (5 H, m, ArH); δ_C 15.9 (Me), 33.6 (CH_2S), 39.5 (CH_2N), 127.2, 128.7, 132.1, 135.3 (ArC), and 169.1 (C=O) ppm; *m/z* 195 (*M*$^+$, 8%), 122 (23), 105 (100), 77 (42), 74 (91), and 51 (13).

3-*Benzoylaminopropanoic acid* (10d)^{15} ν_{max} (Nujol) 3400-3000 (OH and NH), 1700 and 1620 (C=O) cm^{-1}; δ_H 2.6 (2 H, t, *J* 6 Hz, CH_2CO_2), 3.8 (2 H, q, *J* 6 Hz, CH_2N), 7.2-8.2 (5 H, m, ArH), and 8.0-8.2 (2 H, br signal, OH and NH); δ_C 33.6 (CH_2CO_2), 36.7 (CH_2N), 127.4, 129.1, 130.9, 134.8 (ArC), 170.2 (CON), and 177.8 (CO_2) ppm; *m/z* 193 (*M*$^+$, 12%), 105 (100), 88 (13), 77 (32), and 51 (10).

N-(3-*Hydroxy*-4-*methylpentyl)benzamide* (10e) (Found: C, 70.6; H, 8.6; N, 6.2. $C_{13}H_{19}NO_2$ requires C, 70.56; H, 8.65; N, 6.33%) ν_{max} (Nujol) 3320 (OH and NH) and 1630 (C=O) cm^{-1}; δ_H 0.8, 0.85 (6 H, 2 d, *J* 6.5 Hz, 2 x Me), 1.4-1.8 (3 H, m, CH and C*H*$_2$CHO), 3.0-3.2 (1 H, br signal, OH), 3.4 (2 H, q, *J* 5.5 Hz, CH_2N), 3.8 (1 H, q, *J* 5.5 Hz, CHO), 6.9-7.1 (1 H, br signal, NH), and 7.4-8.1 (5 H, m, ArH); δ_C 18.0, 18.9 (2 x Me), 33.1 (*C*H$_2$CHO), 33.7 (*C*HMe), 38.4 (CH_2N), 74.5 (CHO), 127.4, 128.9, 131.3, 134.5 (ArC), and 169.2 (C=O) ppm; *m/z* 221 (*M*$^+$, 2%), 178 (15), 135 (10), 134 (18), 122 (21), 105 (100), and 77 (24).

N-(3-*Hydroxy*-3-*phenylpropyl)benzamide* (10f)^{16} ν_{max} (Nujol) 3310 (OH and NH) and 1630 (C=O) cm^{-1}; δ_H 2.0 (2 H, q, *J* 6.5 Hz, C*H*$_2$CHO), 3.3-3.8 (4 H, m, CH_2N, OH, and NH), 4.8 (1 H, t, *J* 6.5 Hz, CH), and 7.2-8.0 (10 H, m, ArH); δ_C 37.1 (*C*H$_2$CHO), 38.5 (CH_2N), 73.6 (CH), 125.2, 126.1, 126.7, 127.9, 128.3, 131.8, 134.9, 145.3 (ArC), and 169.7 (C=O) ppm; *m/z* 225 (*M*$^+$, 8%),

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When H_2O or D_2O was used as an electrophile a large excess (*ca.* 100 mmol) was added. The carbonation was carried out using an excess of solid carbon dioxide (*ca.* 100 mmol). In the oxydation dry oxygen (purity 99%) precooled at -78 °C was bubbled for 2 h at -78 °C

149 (36), 148 (39), 135 (26), 134 (42), 122 (13), 105 (100), and 77 (41).

N-(*3-Hydroxy-3-methylbutyl)benzamide* (10g)[17] ν_{max} (Nujol) 3360 (OH and NH) and 1630 (C=O) cm^{-1}; δ_H 1.2 (6 H, s, 2 x Me), 1.8 (2 H, t, *J* 6.5 Hz, CH$_2$CO), 2.6-2.8 (1 H, br s, OH), 3.6 (2 H, q, *J* 6.5 Hz, CH$_2$N), 6.9-7.2 (1 H, br signal, NH), and 7.3-8.0 (5 H, m, ArH); δ_C 28.8 (2 x Me), 36.2 (CH$_2$CO), 40.7 (CH$_2$N), 70.4 (COH), 126.9, 128.4, 131.3, 134.9 (ArC), and 168.6 (C=O) ppm; *m/z* 189 (M^+-H$_2$O, 13%), 148 (14), 105 (100), and 77 (36).

N-(*3-Hydroxy-3,3-diphenylpropyl)benzamide* (10h) (Found: C, 79.8; H, 6.3; N, 4.1. $C_{22}H_{21}NO_2$ requires C, 79.73; H, 6.39; N, 4.23%) ν_{max} (Nujol) 3320 (OH and NH) and 1640 (C=O) cm^{-1}; δ_H 1.9-2.1 (1 H, br s, OH), 2.6 (2 H, t, *J* 6.5 Hz, CH$_2$CO), 3.55 (2 H, q, *J* 6.5 Hz, CH$_2$N), 6.7-7.1 (1 H, br signal, NH), and 7.2-7.8 (15 H, m, ArH); δ_C 33.8 (CH$_2$CO), 38.9 (CH$_2$N), 77.3 (COH), 123.9, 125.2, 125.8, 127.1, 127.3, 129.9, 132.8, 145.4 (ArC), and 167.2 (C=O) ppm; *m/z* 331 (M^+, 4%), 254 (12), 183 (21), 150 (15), 149 (86), 148 (66), 105 (100), and 77 (42).

N-(*2-Hydroxyethyl)benzamide* (10i)[14] ν_{max}(neat) 3380 (OH and NH) and 1640 (C=O) cm^{-1}; δ_H 3.3-4.0 (6 H, m, 2 x CH$_2$, OH, and NH), and 7.2-8.1 (5 H, m, ArH); δ_C 43.2 (CH$_2$N), 62.1 (CH$_2$O), 127.2, 128.8, 132.6, 134.9 (ArC), and 169.9 (C=O) ppm; *m/z* 165 (M^+, 3%), 147 (10), 122 (12), 105 (100), 77 (34), and 51 (11).

N-*Propylbenzamide* (11a)[18] ν_{max} (Nujol) 3300 (NH) and 1640 (C=O) cm^{-1}; δ_H 0.9 (3 H, t, *J* 6.5 Hz, Me), 1.55 (2 H, sextet, *J* 6.5 Hz, C*H*$_2$Me), 3.4 (2 H, q, *J* 6.5 Hz, CH$_2$N), 6.35-6.65 (1 H, br signal, NH), and 7.4-8.0 (5 H, m, ArH); δ_C 12.2 (Me), 22.8 (CH$_2$Me), 42.1 (CH$_2$N), 127.4, 128.8, 131.9, 135.6 (ArC), and 169.0 (C=O) ppm; *m/z* 163 (M^+, 16%), 105 (100), 77 (38), and 51 (11).

N-(*3-Deuteriopropyl)benzamide* (11b) ν_{max} (Nujol) 3300 (NH) and 1640 (C=O) cm^{-1}; δ_H 0.9 (2 H, t, *J* 6.5 Hz, CH$_2$D), 1.55 (2 H, quintet, *J* 6.5 Hz, C*H*$_2$CH$_2$D), 3.4 (2 H, q, *J* 6.5 Hz, CH$_2$N), 6.35-6.65 (1 H, br signal, NH), and 7.4-8.0 (5 H, m, ArH); δ_C 12.1 (t, J_{CD} 18.0 Hz, CH$_2$D), 22.8 (CH$_2$CH$_2$D), 42.1 (CH$_2$N), 127.4, 128.8, 131.9, 135.6 (ArC), and 169.0 (C=O) ppm; *m/z* 164 (M^+, 13%), 105 (100), 77 (40), and 51 (15).

N-(*3-Metylthiopropyl)benzamide* (11c)[19] ν_{max} (Nujol) 3340 (NH) and 1640 (C=O) cm^{-1}; δ_H 1.9 (2 H, quintet, *J* 6.5 Hz, C*H*$_2$CH$_2$S), 2.1 (3 H, s, Me), 2.55 (2 H, t, *J* 6.5 Hz, CH$_2$S), 3.55 (2 H, q, *J* 6.5 Hz, CH$_2$N), 6.45-6.75 (1 H, br signal, NH), and 7.2-7.9 (5 H, m, ArH); δ_C 15.3 (Me), 29.3 (CH$_2$CH$_2$S), 31.9 (CH$_2$S), 39.6 (CH$_2$N), 127.2, 129.0, 131.9, 135.3 (ArC), and 168.9 (C=O) ppm; *m/z* 209 (M^+, 8%), 162 (36), 135 (13), 134 (41), 105 (100), 77 (42), and 51 (14).

4-Benzoylaminobutanoic acid (11d)[20] ν_{max} (Nujol) 3400-3000 (OH and NH), 1700, and 1640 (C=O) cm^{-1}; δ_H 1.6-1.8 (2 H, m, C*H*$_2$CH$_2$N), 2.3 (2 H, t, *J* 6.5 Hz, CH$_2$CO$_2$), 3.4 (2 H, t, *J* 7.0 Hz, CH$_2$N), 6.7-6.9 (2 H, br signal, OH and NH), and 7.1-7.7 (5 H, m, ArH); δ_C 25.1 (CH$_2$CH$_2$N), 32.0 (CH$_2$CO$_2$), 40.1 (CH$_2$N), 127.3, 129.2, 131.7, 133.6 (ArC), 168.0 (CON), and 176.4 (CO$_2$) ppm; *m/z* 207 (M^+, 8%), 148 (10), 106 (11), 105 (100), 102 (12), 77 (31), and 51 (10).

N-(*4-Hydroxy-5-metylhexyl)benzamide* (11e) (Found: C, 71.3; H, 9.2; N, 5.8. $C_{14}H_{21}NO_2$

requires C, 71.46; H, 9.00; N, 5.95%) ν_{max} (neat) 3350 (OH and NH) and 1640 (C=O) cm^{-1}; δ_H 0.8 (6 H, d, *J* 6.5 Hz, 2 x Me), 1.2-1.8 (5 H, m, 2 x CH$_2$C and C*H*Me), 2.3-2.4 (1 H, br s, OH), 3.2-3.5 (3 H, m, CH$_2$N and CHO), 6.3-6.6 (1 H, br signal, NH), and 7.1-7.9 (5 H, m, ArH) δ_C 17.9, 19.2 (2 x Me), 26.3, 32.1 (2 x *C*H$_2$C), 34.6 (*C*HMe), 40.4 (CH$_2$N), 76.3 (CHO), 127.2, 128.9, 131.6, 135.2 (ArC), and 169.0 (C=O) ppm; *m/z* 235 (*M*$^+$, 2%), 134 (13), 122 (17), 105 (100), 77 (36), 60 (20), and 43 (10).

N-(*4-Hydroxy-4-phenylbutyl)benzamide* (11f) (Found: C, 76.0; H, 7.2; N, 5.0. $C_{17}H_{19}NO_2$ requires C, 75.81; H, 7.11; N, 5.20%) ν_{max} (neat) 3350 (OH and NH) and 1640 (C=O) cm^{-1}; δ_H 1.4-1.8 (4 H, m, 2 x CH$_2$C), 1.8-1.95 (1 H, br s, OH), 3.4 (2 H, q, *J* 6.5 Hz, CH$_2$N), 4.7 (1 h, t, *J* 5.5 Hz, CH), 6.25-6.55 (1 H, br signal, NH), and 7.1-7.9 (10 H, m, ArH); δ_C 26.1, 36.3 (2 x *C*H$_2$C), 40.8 (CH$_2$N), 74.6 (CH), 125.6, 127.1, 127.4, 128.7, 129.0, 132.1, 135.2, 146.1 (ArC), and 169.1 (C=O) ppm; *m/z* 269 (*M*$^+$, 3%), 163 (20), 162 (11), 148 (15), 135 (10), 134 (26), 122 (18), 105 (100), 79 (12), and 77 (51).

N-(*4-Hydroxy-4-methylpentyl)benzamide* (11g) (Found: C, 70.4; H, 8.8; N, 6.2. $C_{13}H_{19}NO_2$ requires C, 70.56; H, 8.65; N, 6.33%) ν_{max} (neat) 3340 (OH and NH) and 1640 (C=O) cm^{-1}; δ_H 1.2 (6 H, s, 2 x Me), 1.4-1.85 (4 H, m, 2 x CH$_2$C), 1.9-2.0 (1 H, br s, OH), 3.4 (2 H, q, *J* 6.0 Hz, CH$_2$N), 6.4-6.7 (1 H, br signal, NH), and 7.2-7.9 (5 H, m, ArH); δ_C 25.9, 31.2 (2 x *C*H$_2$C), 30.0 (2 x Me), 41.3 (CH$_2$N), 73.8 (COH), 127.2, 129.1, 132.1, 135.2 (ArC), and 168.8 (C=O) ppm; *m/z* 221 (*M*$^+$, 2%), 147 (10), 134 (14), 122 (10), 105 (100), 77 (33), and 59 (12).

N-(*4-Hydroxy-4,4-diphenylbutyl)benzamide* (11h) (Found: C, 80.0; H, 6.7; N, 4.1. $C_{23}H_{23}NO_2$ requires C, 79.97; H, 6.71; N, 4.05%) ν_{max} (Nujol) 3400 (OH and NH) and 1640 (C=O) cm^{-1}; δ_H 1.5-1.8 (3 H, m, C*H*$_2$CH$_2$N and OH), 2.35 (2 H, t, *J* 5.5 Hz, CH$_2$CO), 3.45 (2 H, q, *J* 6.0 Hz, CH$_2$N), 6.2-6.5 (1 H, br signal, NH), and 7.2-7.8 (15 H, m, ArH); δ_C 25.0 (*C*H$_2$CH$_2$N), 38.9 (*C*H$_2$CO), 40.8 (CH$_2$N), 78.7 (COH), 126.7, 127.5, 127.6, 128.9, 129.1, 132.2, 135.6, 148.1 (ArC), and 168.9 (C=O) ppm; *m/z* 345 (*M*$^+$, 2%), 183 (17), 163 (68), 162 (22), 125 (16), 124 (26), 105 (100), and 77 (43).

Acidic Hydrolysis of Compounds (10) or (11). *Isolation of Products* (12)-(14). *General Procedure*.- To a solution of the corresponding compound (10h), (11h), or (11f) (3 mmol) in ethanol (25 ml) and dioxane (10 ml) was added concentrated sulphuric acid (0.5 ml, 9 mmol) and the mixture refluxed for *ca*. 12 h. The cooled solution was evaporated in vacuo (15 mmHg). The resulting residue was treated with water (25 ml) and extracted with ether, the organic layer was neutralized with an aqueous solution of sodium hydroxyde, washed with water, dried (Na_2SO_4), and evaporated in vacuo (15 mmHg). The resulting residue was distilled in vacuo or recrystallized to afford the products (12)-(14).

N-(*3,3-Diphenylprop-2-enyl)benzamide* (12) (0.69 g, 73%) (Found: C, 84.3; H, 6.0; N, 4.4. $C_{22}H_{19}NO$ requires C, 84.31; H, 6.11; N, 4.47%) m.p. 144-145°C (Hexane-CHCl$_3$); ν_{max} (Nujol) 3320 (NH) and 1640 (C=O) cm^{-1}; δ_H 4.1 (2 H, dd, *J* 6.0 and 7.0 Hz, CH$_2$N), 6.1 (1 H, t, *J* 7.0 Hz, CH), 6.5-6.7 (1 H, br signal, NH), and 7.1-7.7 (15 H, m, ArH); δ_C 39.4 (CH$_2$N), 124.5, 126.9, 127.3, 127.5, 128.0, 128.3, 128.4, 129.6, 131.3, 134.3, 138.8, 141.5, 144.4 (ArC and CH=C), and 167.3 (C=O) ppm; *m/z* 313 (*M*$^+$, 14%), 193 (10), 192 (58), 191 (15), 165

(10), 146 (13), 122 (18), 115 (10), 105 (81), 103 (24), 77 (100), and 51 (32).

N-(*4,4-Diphenylbut-3-enyl)benzamide* (13) (0.68 g, 69%) (Found: C, 84.4; H, 6.4; N, 4.2. $C_{23}H_{21}NO$ requires C, 84.38; H, 6.46; N, 4.28%) m.p. 165-167°C (hexane-$CHCl_3$); ν_{max} (Nujol) 3300 (NH) and 1640 (C=O) cm^{-1}; δ_H 2.5 (2 H, q, *J* 7.0 Hz, CH_2CH), 3.55 (2 H, q, *J* 7.0 Hz, CH_2N), 6.1 (1 H, t, *J* 7.0 Hz, CH), 6.3-6.5 (1 H, br signal, NH), and 7.1-7.7 (15 H, m, ArH); δ_C 28.2 (CH_2CH), 37.6 (CH_2N), 124.5, 126.8, 127.3, 127.4, 128.1, 128.3, 128.4, 129.6, 131.2, 134.3, 138.9, 141.5, 144.5 (ArC and CH=C), and 167.5 (C=O) ppm; *m/z* 327 (M^+, 5%), 207 (17), 206 (91), 205 (17), 191 (22), 178 (15), 165 (12), 149 (10), 115 (32), 105 (100), 91 (36), 77 (54), and 51 (13).

3-*Phenylpyrrolidine* (14) (0.26 g, 59%) b.p. 101-103°C (0.1 mmHg) [Lit.,[24] 241 (771 mmHg)]; ν_{max} (neat) 3400 (NH) cm^{-1}; δ_H 1.6-2.1 (4 H, m, 2 x CH_2C), 2.9-3.1 (2 H, m, CH_2N), 3.4-3.6 (1 H, br s, NH), 4.1 (1 H, t, *J* 7.0 Hz, CH), and 7.1-7.5 (5 H, m, ArH); δ_C 25.3, 34.7 (2 x CH_2C), 46.7 (CH_2N), 64.3 (CH), 126.0, 126.8, 128.6, and 143.9 (ArC) ppm; *m/z* 147 (M^+, 27%), 146 (48), 119 (21), 118 (100), 104 (12), 91 (11), 77 (10), and 70 (21).

Basic Hydrolysis of Compound (11h). *Isolation of* 4-*Amino*-1,1-*diphenylbutan*-1-*ol* (15).- A solution of *N*-(3-hydroxy-3,3-diphenylpropyl)benzamide (1.0 g, 3 mmol) and potassium hydroxide (0.74 g, 15 mmol) in water (10 ml), ethanol (15 ml), and dioxane (10 ml) was refluxed for *ca*. 12 h. The cooled mixture was extracted with ether, the organic layer washed with water, dried (Na_2SO_4), and evaporated in vacuo (15 mmHg). The resulting residue was recrystallized to afford the titled (15) (0.59 g, 81%) (Found: C, 79.7; H, 7.8; N, 5.7. $C_{16}H_{19}NO$ requires C, 79.63; H, 7.94; N, 5.80%) m.p. 67-69°C (hexane-$CHCl_3$); ν_{max} (Nujol) 3350 (OH and NH) cm^{-1}; δ_H 1.4 (2 H, quintet, *J* 6.0 Hz, CH_2CH_2N), 2.3 (2 H, t, *J* 6.0 Hz, CH_2CO), 2.6 (2 H, t, *J* 6.0 Hz, CH_2N), 3.5-3.7 (3 H, br s, OH and NH_2), and 7.0-7.4 (10 H, m, ArH); δ_C 26.7 (CH_2CH_2N), 41.1, 41.5 (CH_2CO and CH_2N), 76.6 (CO), 126.1, 127.8, and 148.0 (ArC) ppm; *m/z* 241 (M^+, 10%), 183 (25), 180 (21), 147 (14), 106 (12), 105 (100), 91 (10), 77 (61), 59 (47), and 51 (10).

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